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Interplay between the palladium(II) ion, unidentate ligands and hydroxyl groups from a bidentate ligand in a new complex that catalyses hydration and alcoholysis of nitrile and urea ‡

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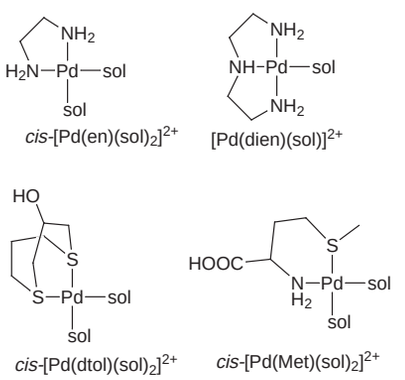
Palladium(II) complexes containing the bidentate ligand 3,6-dithiaoctane-1,8-diol (dtod) and chloride anions (**1**) or solvent molecules (**2**) as two unidentate ligands were synthesized and characterized by ^{1}H and ^{13}C NMR spectroscopy. The complex **1**, which is the precursor to the catalyst **2**, was also characterized by elemental analysis and X-ray crystallography. The crystal structure of **1** shows square planar co-ordination of two sulfur and two chloride ligands to palladium(II), and also a hydrogen bonding network. The complex **2** catalyses hydration of dichloroacetonitrile to dichloroacetamide and methanolysis of dichloroacetonitrile to (dichloromethyl)methoxymethanimine. The catalysed reactions are as much as 10^6 times faster than the uncatalysed ones. The hydroxyl groups in the ligand dtod do not directly participate in the hydration and methanolysis reactions of dichloroacetonitrile catalysed by **2**. The nitrile is activated for nucleophilic attack by its co-ordination to palladium(II). The nucleophile is the free water molecule or the aqua ligand in the hydration reaction and the free methanol molecule in the methanolysis reaction. Indeed, the latter reaction is first order with respect to methanol concentration. Urea and methylurea co-ordinated to palladium(II) in the complex **2** react with the hydroxyl groups of the dtod ligand and form alkyl carbamates. This unimolecular alcoholysis within the co-ordination sphere of palladium(II) is 240–380 times faster than the bimolecular alcoholysis involving external attack of free ethanol.

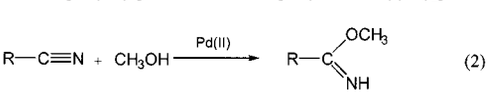
Introduction

Palladium complexes are well known reagents and catalysts in organic synthesis.[1] We recently reported the use of various palladium(II) aqua complexes as catalysts for the hydration of nitriles.[2] These complexes, some of which are shown below, also catalyse hydrolytic cleavage of peptides, decomposition of urea to carbon dioxide and ammonia, and alcoholysis of urea to ammonia and various carbamate esters.[3–5] Clearly, palladium(II) aqua complexes are versatile catalysts for hydrolytic reactions. Their catalytic properties arise from the presence of labile water or other solvent ligands which can be displaced by a substrate. In many cases the co-ordinated substrate becomes activated toward nucleophilic additions of water/hydroxide or alcohols. If the catalyst is a diaqua complex, the aqua ligand remaining after the entry of the substrate deprotonates at a relatively low pH (pK_a = 3–6), and the hydroxide ligand can act as a nucleophile or general base catalyst. Therefore, the search for new palladium(II) complexes that bind and activate organic substrates is likely to result in more efficient catalysts.

Here we report on new palladium(II) complexes *cis*-[Pd(dtod)Cl$_2$] **1** and *cis*-[Pd(dtod)(sol)$_2$]$^{2+}$ **2**, containing bidentate ligand 3,6-dithiaoctane-1,8-diol (dtod) and unidentate ligands chloride anions or the solvent (sol) molecules. The complex **2** is an efficient catalyst for the hydration and methanolysis of nitriles, reactions shown in eqns. (1) and (2). Alcoholysis of nitriles

(1)





(2)

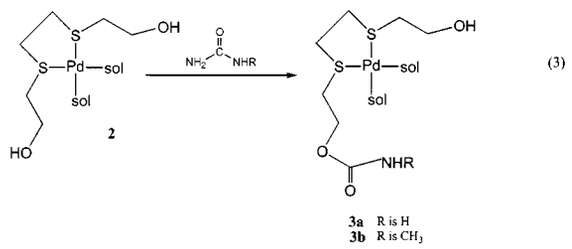
catalysed by palladium(II) complexes has not been described before. The complex *cis*-[Pd(dtod)(sol)$_2$]$^{2+}$ also promotes stoichiometric alcoholysis of urea by the hydroxyl groups within the ligand dtod, as shown in eqn. (3). We compare the rates of this unimolecular reaction within the co-ordination sphere of palladium(II) and of bimolecular ethanolysis of urea.

Experimental

Chemicals

The deuterium-containing compounds D_2O and $DClO_4$, the salts $K_2[PdCl_4]$, $PdCl_2$ and $AgClO_4 \cdot H_2O$, and the reactants

† For correspondence regarding X-ray crystallographic studies.
‡ *Supplementary data available*: figure showing the hydrogen-bond network in complex **1**. Available from BLDSC (No. SUP 57445, 2 pp.) or the RSC Library. See Instructions for Authors, 1998, Issue 1 (http://www.rsc.org/dalton).



(3)

$CHCl_2CN$, $NHCH_3C(O)NH_2$ and $(NHCH_3)_2CO$ were obtained from Sigma Chemical Co. and Aldrich Chemical Co. The isotopomers of urea $(^{15}NH_2)_2CO$ (^{15}N 98%) and $(NH_2)_2{}^{13}CO$ (^{13}C 99%) were from Cambridge Isotope Laboratories, anhydrous $AgBF_4$ and $AgClO_4$ (**CAUTION:** strong oxidant!) from G. Frederich Smith Chemical Co, the ligands ethane-1,2-diamine (en), 1,5-dithiacyclooctan-3-ol (dtcol) and 3,6-dithiaoctane-1,8-diol (dtod) from Aldrich Chemical Co. and $(CD_3)_2CO$, CD_3OD and $DCON(CD_3)_2$ from Cambridge Isotope Laboratories. These and all other chemicals were of reagent grade.

Palladium(II) complexes

The palladium(II) complexes *cis*-$[Pd(en)Cl_2]$ and *cis*-$[Pd(dtcol)Cl_2]$ were prepared by the published procedures.[6] The chloro ligands were displaced by the solvent ligands (sol) by stirring solutions of these complexes and 2 equivalents of $AgBF_4$, $AgClO_4$ or $AgClO_4{\cdot}H_2O$ in $(CD_3)_2CO$, for 1 h at 25 °C, in the dark. The solid AgCl was filtered off in the dark, and a fresh solution of the solvent complex was used in further experiments. The salt *cis*-$[Pd(en)(sol)_2][ClO_4]_2$ had the absorption maximum at 360 nm, as reported before.[6] The complex *trans*-$[Pd(PhCN)_2Cl_2]$ was prepared by the published procedure.[7] The complex *cis*-$[Pd(dtod)Cl_2]$ **1** was prepared from *trans*-$[Pd(PhCN)_2Cl_2]$ and 1 equivalent of 3,6-dithiaoctane-1,8-diol in benzene at room temperature. The mixture was stirred overnight, and the yellow precipitate was filtered off. The solid is soluble in dimethylformamide and acetone. Isolated yield 26% {Found: C, 20.53; H, 3.91. Calc. for *cis*-$[Pd(dtod)Cl_2]$: C, 20.04; H, 3.92%}. ^{13}C NMR at 293 K in $HCON(CD_3)_2$: δ 60.5, $2CH_2$; 41.0, CH_2; 40.6, CH_2; 39.3, CH_2; 39.0, CH_2. ^{13}C NMR in $HCON(CD_3)_2$ at 313 K: δ 60.5, $2CH_2$; 40.8, $2CH_2$; 39.15, $2CH_2$. The chloride ligands in the complex **1** were solvated by stirring a solution of **1** and 2 equivalents of $AgBF_4$, $AgClO_4$ or $AgClO_4{\cdot}H_2O$ in $(CD_3)_2CO$ for 1 h at 25 °C, in the dark. The solid AgCl was filtered off in the dark, and a fresh solution of the solvent complex was used. ^{13}C NMR of *cis*-$[Pd(dtod)(sol)_2]^{2+}$ in $(CD_3)_2CO$ at 313 K: δ 59.5, $2CH_2$; 41.6, $2CH_2$; 39.2, $2CH_2$. The co-ordinated solvent (sol) is $(CD_3)_2CO$, H_2O/D_2O, CD_3OD or C_2D_5OD.

Crystal and molecular structure of *cis*-$[Pd(dtod)Cl_2]$ 1

Crystallographic details are given in Table 1. The systematic absences in the diffraction data were consistent with space groups $P1$ and $P\bar{1}$. The E statistics strongly suggested the centrosymmetric space group $P\bar{1}$ which yielded chemically reasonable and computationally stable results of refinement. The structure was solved using direct methods, completed by subsequent Fourier-difference synthesis, and refined by using full-matrix, least-squares procedures. The empirical absorption corrections were applied by the program DIFABS.[8] All non-hydrogen atoms were refined with anisotropic displacement coefficients. All hydrogen atoms were treated as idealized contributions. All software and sources of the scattering factors are contained in the SHELXTL (version 5.03) program library.[9]

CCDC reference number 186/1208.

Proton and carbon-13 NMR spectra

These spectra were recorded with Varian VXR-300 and Bruker DRX-400 spectrometers. The chemical shifts (δ) are given in ppm downfield from the methyl resonance of the solvent, which was $(CD_3)_2CO$. The internal reference in ^1H NMR kinetic experiments was tetramethylsilane. The internal reference in ^{13}C NMR kinetic experiments performed in $(CD_3)_2CO$ was the carbonyl resonance of this solvent because its chemical shift is similar to the shifts of urea and of the carbamate esters. The quality of the ^{13}C NMR spectra was improved by their acquisition in narrow windows. In all the quantitative experiments the solution was made 0.040 M in $[Cr(acac)_3]$. The delay between the pulses was longer than $5T_1$ for the slowest-relaxing species, CO_2; each scan took 9.35 s. Usually 3000–6000 scans were taken. Spectra were recorded with and without proton decoupling. In quantitative experiments, in which accurate relative intensities were needed, decoupling was not used. The proton and carbon-13 resonances were integrated with an estimated error of ±5 and 10%, respectively. Concentrations of the compounds were determined on the basis of these integrals and the known initial concentrations of reagents. Equilibrium constants, rates and rate constants were calculated from the known concentrations of the reactants and products, with an estimated error of 10–20%.

Kinetics of reactions

The following solvents were used in experiments with dichloroacetonitrile ($CHCl_2CN$): a 9.3 M solution of D_2O in $(CD_3)_2CO$ in experiments concerning hydration and solutions of CD_3OD in $(CD_3)_2CO$ in experiments concerning methanolysis. The temperature was always 313 ± 0.5 K. The initial concentrations of a palladium(II) complex and $CHCl_2CN$ were 0.017 and 0.17 M, respectively, unless stated otherwise. The reactions in eqns. (1) and (2) were followed by ^1H NMR spectroscopy. In a typical experiment, to a solution of a freshly prepared complex was added neat $CHCl_2CN$ to start the reaction, and the acquisition began within less than a minute. The solvent in experiments concerning alcoholysis of urea by *cis*-$[Pd(dtod)(sol)_2]^{2+}$ was always $(CD_3)_2CO$. The reactions in eqn. (3) were followed by ^1H and ^{13}C NMR spectroscopy. The solvent in experiments concerning ethanolysis of urea catalysed by *cis*-$[Pd(en)(sol)_2]^{2+}$ was a 1.5 M solution of C_2D_5OD in $(CD_3)_2CO$. Catalytic ethanolysis was followed by ^{13}C NMR spectroscopy. In a typical ^1H NMR spectroscopy experiment, to a solution of a freshly prepared complex was added solid urea, to start the reaction. Acquisition of spectra at 313 ± 0.5 K began within less than one minute after mixing. In a typical ^{13}C NMR spectroscopy experiment, to a solution of a freshly prepared complex were added solid $[Cr(acac)_3]$ and solid urea, to start the reaction. The final concentrations of a palladium(II) complex, urea and $[Cr(acac)_3]$ were 0.30, 0.30 and 0.040 M, respectively. The reaction mixture was incubated at 313 ± 0.5 K in the NMR tube. After every 5–10 min the NMR tube was cooled to 273 K and ^{13}C NMR spectra at 273 K were taken.

The initial rates were determined in experiments in which only the first 3–5% of the reaction were followed. The observed rate constants were determined from the initial rates.

Composition of the reaction mixtures

The reactants were dichloroacetonitrile and urea (or methylurea and 1,3-dimethylurea) and the products were dichloroacetamide [eqn. (1)], (dichloromethyl)methoxymethanimine [eqn. (2)], ammonia, ammonium ion, methylamine, ethyl carbamate, ethyl *N*-methylcarbamate and complexes **3a** and **3b**, containing carbamate esters of the ligand dtod [eqn. (3)]. All of these compounds (except NH_3/NH_4^+ ion and methylamine) were detected by ^1H or ^{13}C NMR spectroscopy. Proton NMR data (δ in ppm): $CHCl_2CN$, 7.09; $CHCl_2C(O)NH_2$, 6.23; $CHCl_2C(OCH_3)NH$, 6.45; for the nitrile ligand in *cis*-$[Pd(dtod)(sol)(CHCl_2CN)]^{2+}$, 7.9 (s); CH_2 in complex **3b**, 3.7 (t), 3.1 (t), and 2.64 (d). Carbon-13 NMR data (δ in ppm): $NH_2C(O)NH_2$,

162.8; $NH_2C(O)NHCH_3$, 161.5 and 27.0 (q); $NHCH_3C(O)NHCH_3$, 161.1 and 27.3 (q); for the urea ligand, 158.0 in *cis*-$[Pd(en)(H_2O)\{NH_2C(O)NH_2\}]^{2+}$, 165.5 in *cis*-$[Pd(en)(H_2O)\{OC(NH_2)_2\}]^{2+}$, 157.9 in *cis*-$[Pd(en)(H_2O)\{NH_2C(O)NHCH_3\}]^{2+}$ [CH_3 resonance overlaps with that of $(CD_3)_2CO$], 164.5 and 28.5 (q) in *cis*-$[Pd(en)(H_2O)\{OC(NH_2)(NHCH_3)\}]^{2+}$, 163.7 and 27.3 (q) in *cis*-$[Pd(en)(H_2O)\{OC(NHCH_3)_2\}]^{2+}$, 156.8 in *cis*-$[Pd(dtod)(sol)\{NH_2C(O)NH_2\}]^{2+}$, 164.8 in *cis*-$[Pd(dtod)(sol)\{OC(NH_2)_2\}]^{2+}$, 157.9 and 31.9 (q) in *cis*-$[Pd(dtod)(sol)\{NH_2C(O)NHCH_3\}]^{2+}$, 163.2 and 31.0 (q) in *cis*-$[Pd(dtod)(sol)\{OC(NH_2)(NHCH_3)\}]^{2+}$, 163.0 and 28.0 (q) in *cis*-$[Pd(dtod)(sol)\{OC(NHCH_3)_2\}]^{2+}$; CH_2 in complex **3a**, 61.0, 39.0 and 37.5; C(O) in complex **3a**, 156.1; CH_2 in complex **3b**, 59.3, 39.0 and 36.0; C(O) in complex **3b**, 153.8; CH_3 in complex **3b**, 28.0; for C(O), 157.0 in $NH_2C(O)OC_2H_5$, 155.8 in $NHCH_3C(O)OC_2H_5$. Assignments of resonances were confirmed by spiking the reaction mixture with the pure chemical of interest, if this chemical was commercially available. The chemical shifts could deviate from the stated values by 0.10 ppm or less, depending on the composition of the reaction mixture and other conditions. Dichloroacetamide and (dichloromethyl)-methoxymethanimine were obtained as $CHCl_2C(O)ND_2$ and $CHCl_2C(OCD_3)ND$, respectively; for the sake of consistency, they are shown as $CHCl_2C(O)NH_2$ and $CHCl_2C(OCH_3)NH$ in schemes and equations.

Results and discussion

Synthesis and characterization of *cis*-[Pd(dtod)Cl_2] 1 in solution

The ligand 3,6-dithiaoctane-1,8-diol slightly resembles in structure and solubility 1,5-dithiacyclooctan-3-ol (dtcol), complexes of which have previously been described.[6b] Therefore, we chose a synthetic route for *cis*-[Pd(dtod)Cl_2] which is similar to that for *cis*-[Pd(dtcol)Cl_2].[6b] The isolated yield is relatively low because the five-membered ring in complex **1** is sterically hindered.[10] Since an orange oil is always a side product, we concluded that dtod can also bridge palladium(II) ions, forming polynuclear complexes.

Variable-temperature ^{13}C NMR spectra of complex **1** showed fluxional behaviour. There are five resonances at 293 K, at δ 60.5, 41.0, 40.6, 39.3 and 39.0, but only three at 313 K, at δ 60.5, 40.8 and 39.15. Since complex **1** does not racemize at 293 K, it exists in two enantiomeric and one *meso* forms, which are distinguishable by ^{13}C NMR spectroscopy.[11] The coalescence at 313 K can be attributed to the increased rate of intramolecular inversion at the sulfur atom.[12,13]

Molecular structure and hydrogen bonding in *cis*-[Pd(dtod)Cl_2] 1

The palladium(II) atom in complex **1** sits in a square planar environment. The average Pd–Cl and Pd–S distances are 2.327(2) and 2.266(3) Å, respectively, similar to the average values of 2.317(12) and 2.264(11) Å found in similar complexes;[14–19] see Fig. 1 and Table 2. The palladium(II) ion also interacts with the distal atom Cl(1′) ($-x$, $-y$, $1-z$), located above the co-ordination plane, 3.670(6) Å, and the corresponding vector forms an angle of 173.9(8)° with the plane defined by atoms Cl(1), Cl(2), S(1) and S(2). Atom Cl(1) also forms a hydrogen bond with H(2A)–O(2) ($x+1$, y, z); the Cl(1)···O(2) distance is 3.139(9) Å and the Cl(1)–H(2A)–O(2) angle is 153.1(8)°. Atom Cl(2), however, does not form intermolecular bonds. In the hydrogen bond O(1)–H(1A)···O(2^1) (x, $y-1$, $z+1$) formed between hydroxyl groups of two adjacent molecules the O(1)···O(2^1) distance is 2.742(7) Å and the angle is 169.0(8)°.

Formation of *cis*-[Pd(dtod)$(sol)_2$]$^{2+}$

The chloride ligands in *cis*-[Pd(dtod)Cl_2] were displaced by the solvent [D_2O, $(CD_3)_2CO$, CD_3OD or ethanol] during treatment with $AgClO_4$ or $AgBF_4$ salts. Upon heating the complex *cis*-$[Pd(dtod)(sol)_2]^{2+}$, prepared in organic solvents, slowly decomposes. Its stability is increased if 2 equivalents of water per complex are added to the organic solvent. Since ^{13}C NMR spectra of complexes **1** and **2** are very similar, we conclude that hydroxyl groups do not co-ordinate to palladium(II) upon the displacement of chloride ligands and remain available for alcoholysis reactions.

Table 1 Crystallographic data for complex **1**

Formula	$C_6H_{14}Cl_2O_2PdS_2$
Formula weight	359.59
Space group	$P\bar{1}$
a/Å	8.549(2)
b/Å	8.784(2)
c/Å	9.326(2)
α/°	62.26(3)
β/°	71.27(3)
γ/°	81.58(3)
V/Å^3	586.3(2)
Z	2
Crystal colour, habit	Yellow rod
D_c/g cm^{-3}	2.037
μ(Mo-Kα)/cm^{-1}	23.61
T/K	296(2)
Absorption corrections	Empirical
T(max)/T(min)	1.000/0.616
Diffractometer	CAD4
Reflections collected	2208
Independent reflections (R_{int})	2004 (0.01)
Observed reflections [$I > 2\sigma(I)$]	1792
$R(F)$	0.0237
$R(wF^2)$	0.0603

Table 2 Selected bond lengths (Å) and angles (°) for complex **1**

Pd(1)–S(2)	2.2643(10)	Pd(1)–S(1)	2.2682(14)
Pd(1)–Cl(1)	2.3252(15)	Pd(1)–Cl(2)	2.3289(11)
S(2)–Pd(1)–S(1)	90.05(4)	S(2)–Pd(1)–Cl(1)	87.49(4)
S(1)–Pd(1)–Cl(1)	171.92(3)	S(2)–Pd(1)–Cl(2)	176.85(3)
S(1)–Pd(1)–Cl(2)	88.16(4)	Cl(1)–Pd(1)–Cl(2)	94.63(4)

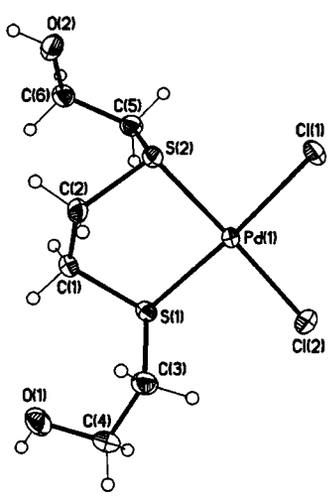


Fig. 1 An ORTEP[20] drawing of *cis*-[Pd(dtod)Cl_2] **1**. The thermal ellipsoids of the non-hydrogen atoms are drawn at 30% probability level. Hydrogen atoms were set in calculated positions, and their thermal ellipsoids have an arbitrary scale.

Nitrile hydration

Hydration of nitriles and the formation of corresponding carboxamides [eqn. (1)] is an important reaction both in the laboratory and in industry.[21,22] This reaction is catalysed by various acids and bases, but many of these classical methods require harsh conditions and give low yields.[23] Further

Table 3 Hydration of $CHCl_2CN$ catalysed by the two palladium(II) complexes[a]

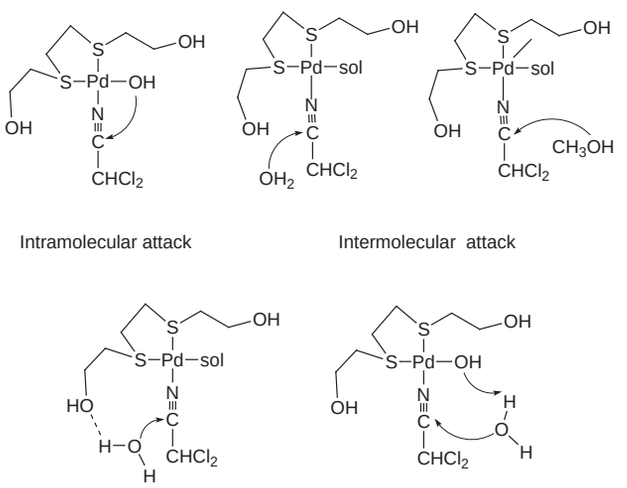
Catalyst	$10^3 k_{obs}$/M min^{-1}
cis-[Pd(dtcol)(sol)$_2$]$^{2+}$	0.830 ± 0.160[b]
cis-[Pd(dtod)(sol)$_2$]$^{2+}$	2.74 ± 0.88

[a] Initial concentrations of the catalyst and $CHCl_2CN$ were 0.017 and 0.17 M, respectively, the solvent was 9.3 M D_2O in $(CD_3)_2CO$, and the temperature was 313 K. [b] From ref. 2.

hydrolysis of carboxamides into carboxylic acids cannot be avoided, because this undesirable reaction is faster than hydration, especially under basic conditions. Extreme acidity and basicity can be avoided if transition-metal complexes are used.[2,24–27]

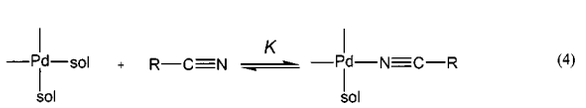
We recently showed that complexes illustrated in the Introduction catalyse selective hydration of various nitriles to carboxamides, as in eqn. (1).[2] The hydration rate increases as the electron-withdrawing ability of the substituents R increases in a series of similar nitriles: CH_3CN, CH_2ClCN, $CHCl_2CN$ and CCl_3CN. Trichloroacetonitrile could not be used in kinetic studies because it lacks protons required for detection by ^{1}H NMR spectroscopy, and because its hydration is too fast to be followed by ^{13}C NMR spectroscopy.[2] Therefore, we chose $CHCl_2CN$, hydration of which can be conveniently followed by ^{1}H NMR spectroscopy.

The complex *cis*-[Pd(dtod)(sol)$_2$]$^{2+}$ efficiently catalyses selective hydration of dichloroacetonitrile to dichloroacetamide under mild conditions. As Table 3 shows, it is three times more reactive than the structurally similar complex *cis*-[Pd(dtcol)(sol)$_2$]$^{2+}$.[2] The presence of hydroxyl groups in close proximity to activated nitrile and an aqua ligand in *cis*-[Pd(dtod)(sol)$_2$]$^{2+}$ may slightly enhance the reaction rate by general base catalysis, as shown in Scheme 1.



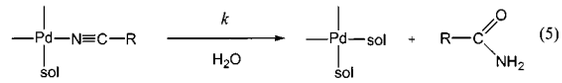
Scheme 1 Catalytic mechanisms.

Binding of various nitriles to palladium(II) complexes, shown in eqn. (4), was studied by ^{1}H NMR spectroscopy.[2] A chloro


(4)

substituent in the nitrile, by its inductive effect, lowers the binding constant approximately ten-fold. Co-ordination of $CHCl_2CN$ causes a 0.81 ppm chemical shift downfield of the ^{1}H NMR resonance. This large change allowed determination of the equilibrium constant *K*, which could only be estimated in our previous study.[2] For *cis*-[Pd(dtod)(sol)$_2$]$^{2+}$ and $CHCl_2CN$, the value is 0.98 ± 0.30 M^{-1} at 313 K.

Dichloroacetonitrile becomes more electrophilic upon co-ordination and undergoes fast hydration, yielding dichloroacetamide; see eqn. (5). The rate constant *k*, determined by


(5)

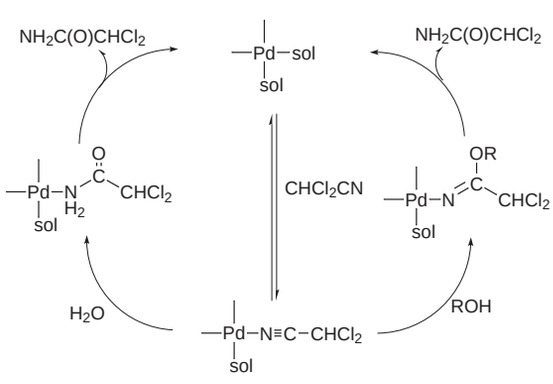
eqn. (6) from the known initial concentrations of *cis*-[Pd-

$$k_{obs} = Kk[cis\text{-Pd(dtod)(sol)}_2^{2+}][D_2O] \qquad (6)$$

(dtod)(sol)$_2$]$^{2+}$ and D_2O and *K*, is $(1.76 \pm 0.56) \times 10^{-2}$ M^{-1} min^{-1}.

Various experiments showed that acetamide and dichloroacetamide do not detectably bind to *cis*-[Pd(dtod)(sol)$_2$]$^{2+}$ in the presence of 9.3 M D_2O (the conditions used for hydration reactions) or in neat $(CD_3)_2CO$. This finding, that the carboxamides are labile ligands to palladium(II), rules out inhibition of nitrile hydration by co-ordination of the product, carboxamide, to the catalyst. Without the inhibition, the catalysts are more efficient and the attainable turnover numbers are high. For instance, as much as 1000 equivalents of dichloroacetonitrile are hydrated by 1 equivalent of the palladium(II) complex.[2] Since there is no inhibition or decomposition of the palladium(II) catalyst, even higher concentrations of nitriles can be converted into the respective amides.

Palladium(II) catalysts containing various bidentate ligands use the same mechanism for nitrile hydration.[2] Owing to the close similarities in structure and reactivity between the new complex *cis*-[Pd(dtod)(sol)$_2$]$^{2+}$ and those studied previously, we conclude that they operate by the same mechanism, shown in Scheme 2. Nitrile becomes activated upon co-ordination to



Scheme 2 Hydration and alcoholysis of $CHCl_2CN$.

palladium(II). Water or hydroxide ion attacks co-ordinated nitrile either internally or externally, as shown in Scheme 1. These two mechanisms are kinetically indistinguishable, because no intermediates were observed in this study. Co-ordinated carboxamide is labile and is readily displaced by the solvent. Hydration catalysed by *cis*-[Pd(dtod)(sol)$_2$]$^{2+}$ is as much as 10^6 times faster than the uncatalysed reaction. Reaction in the absence of the palladium(II) catalyst was carried out under similar conditions, such as temperature, solvent composition, and concentrations of the nitrile and acid, as the reaction in its presence. Periodically the progress in the background hydration was checked by ^{1}H NMR spectroscopy. Even after 13 months incubation at 313 K, no resonance of the hydration product, dichloroacetamide, was detected. Therefore, the observed rate constant for the background reaction was estimated on the basis of the sensitivity of the NMR spectra.

Table 4 Methanolysis of $CHCl_2CN$ catalysed by various palladium(II) complexes *

Catalyst	$10^3 k_{obs}/min^{-1}$
cis-$[Pd(dtod)(sol)_2]^{2+}$	5.05 ± 0.62
cis-$[Pd(dtcol)(sol)_2]^{2+}$	2.38 ± 0.23
cis-$[Pd(en)(sol)_2]^{2+}$	3.62 ± 0.08

* Initial concentrations of the catalyst and of $CHCl_2CN$ were 0.017 and 0.17 M, respectively, the solvent was 9.3 M CD_3OD in $(CD_3)_2CO$ and the temperature was 313 K.

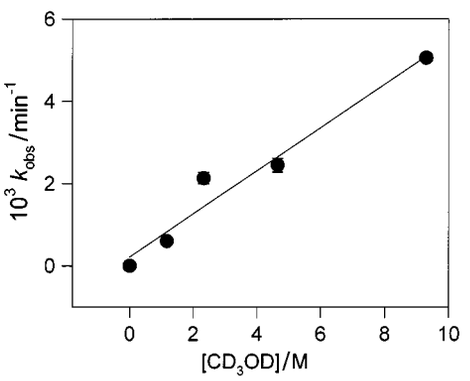


Fig. 2 Observed rate constant for methanolysis of $CHCl_2CN$ catalysed by *cis*-$[Pd(dtod)(sol)_2]^{2+}$ as a function of the concentration of CD_3OD in $(CD_3)_2CO$ as a solvent. The initial concentrations of $CHCl_2CN$ and the catalyst were 0.17 and 0.017 M, respectively. The temperature was 313 K. Error bars for some of the values are smaller than the point symbols.

Nitrile methanolysis

Alcohols have basic and nucleophilic properties similar to those of water and are potential reagents for various reactions.[28] Surprisingly, alcoholysis of nitriles has not been studied in detail,[29–32] and to our knowledge palladium(II) complexes have not been used as catalysts for this reaction. The complexes illustrated in the Introduction and also *cis*-$[Pd(dtod)(sol)_2]^{2+}$ efficiently catalyse methanolysis of dichloroacetonitrile to (dichloromethyl)methoxymethanimine. As Table 4 shows, similar complexes show similar reactivity.

Since the concentrations of CD_3OD in the methanolysis experiments and of D_2O in the hydration experiments were both 9.3 M, the corresponding results can be directly compared. The following values were obtained with the new catalyst *cis*-$[Pd(dtod)(sol)_2]^{2+}$. The respective binding constants K are 1.9 ± 0.6 M^{-1} in the presence of CD_3OD and 0.98 ± 0.30 M^{-1} in the presence of D_2O; the respective second-order rate constants are identical, $(1.70 \pm 0.18) \times 10^{-2}$ and $(1.76 \pm 0.56) \times 10^{-2}$ M^{-1} min^{-1}.

Since the palladium(II) catalysts in Table 4 are always synthesized in the solvent containing 2 equivalents of water per catalyst, and hydration and methanolysis have identical rate constants, hydration occurs as a minor side reaction in a 9.3 M solution of CD_3OD in $(CD_3)_2CO$. Addition of CD_3OD enhances methanolysis and inhibits hydration, as Figs. 2 and 3 show. First-order behaviour with respect to $[CD_3OD]$ indicates intermolecular reaction between co-ordinated dichloroacetonitrile and free CD_3OD, shown in Schemes 1 and 2.

The overall mechanism of nitrile methanolysis, shown in Scheme 2, is consistent with the experimental results. Rapid binding and activation of dichloroacetonitrile is followed by intermolecular addition of methanol. Fast dissociation of the product, (dichloromethyl)methoxymethanimine, restores the catalyst. The rate enhancement in the presence of palladium(II) complexes is at least 10^6-fold relative to the uncatalysed methanolysis. The estimated rate constant for the latter was

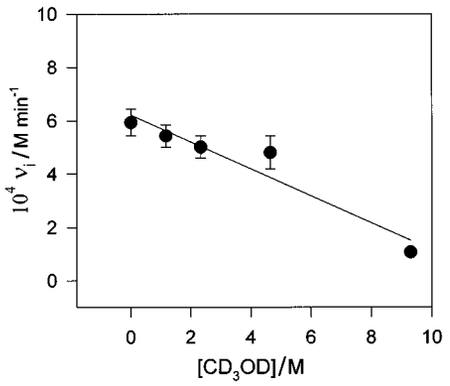
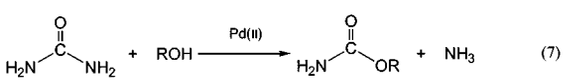


Fig. 3 Initial rate for hydration of $CHCl_2CN$ catalysed by *cis*-$[Pd(dtod)(sol)_2]^{2+}$ as a function of the concentration of CD_3OD in $(CD_3)_2CO$ as a solvent. Other details as in Fig. 2.

determined similarly to the rate constant for the background hydration of nitriles.

Urea alcoholysis

In the presence of some palladium(II) complexes urea undergoes catalytic alcoholysis according to eqn. (7), yielding



(7)

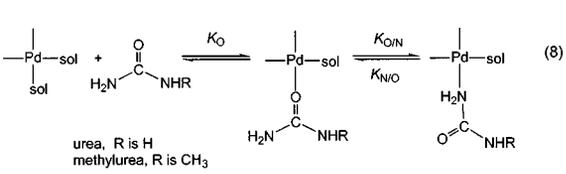
carbamate esters and ammonia.[5] This reaction is at least 10^5 times faster than the uncatalysed alcoholysis under the same conditions.

Since the hydroxylic groups in the ligand dtod in the *cis*-$[Pd(dtod)(sol)_2]^{2+}$ complex do not co-ordinate to palladium(II) they can react with co-ordinated urea. Although there is no turnover, these reactions are interesting because the substrate and the nucleophile exist within the same complex, but only the substrate is co-ordinated to the metal atom.

Equilibrium constants for urea co-ordination to palladium(II)

In $(CD_3)_2CO$ solutions urea and methylurea bind to *cis*-$[Pd(dtod)(sol)_2]^{2+}$ *via* the O atom or the N atom, as shown in Scheme 3. Both linkage isomers were detected and characterized by ^{13}C NMR spectroscopy. Complexes in which the methylated N atom of methylurea is co-ordinated to palladium(II) have not been detected by ^{13}C NMR spectroscopy. Our finding corroborates a previous report that monosubstituted ureas yielded exclusively the N-bonded isomers $[Co(NH_3)_5\{NHC(O)NHR\}]^{2+}$ and not $[Co(NH_3)_5\{NRC(O)NH_2\}]^{2+}$.[33,34]

Urea and methylurea initially displace a solvent ligand in complexes *cis*-$[Pd(dtod)(sol)_2]^{2+}$ and *cis*-$[Pd(en)(sol)_2]^{2+}$ to yield the O-bound isomer, which then converts into the N-bound isomer. With *cis*-$[Pd(dtcol)(sol)_2]^{2+}$ this conversion occurs over approximately an hour, but further decomposition of N-bound urea into ammonia and carbon dioxide precluded accurate determinations of the rate constants.[4] Similarly, O-bound urea in the $[Pt(dien)\{OC(NH_2)(NMe_2)\}]^{2+}$ complex isomerizes to N-bound urea with a half-life of 20 min.[35] The two equilibrium constants for the initial co-ordination (K_O), for ligand isomerizations ($K_{O/N}$ and $K_{N/O}$), and for stepwise formation of the N-bound linkage isomer (K_N) are defined in eqns. (8) and

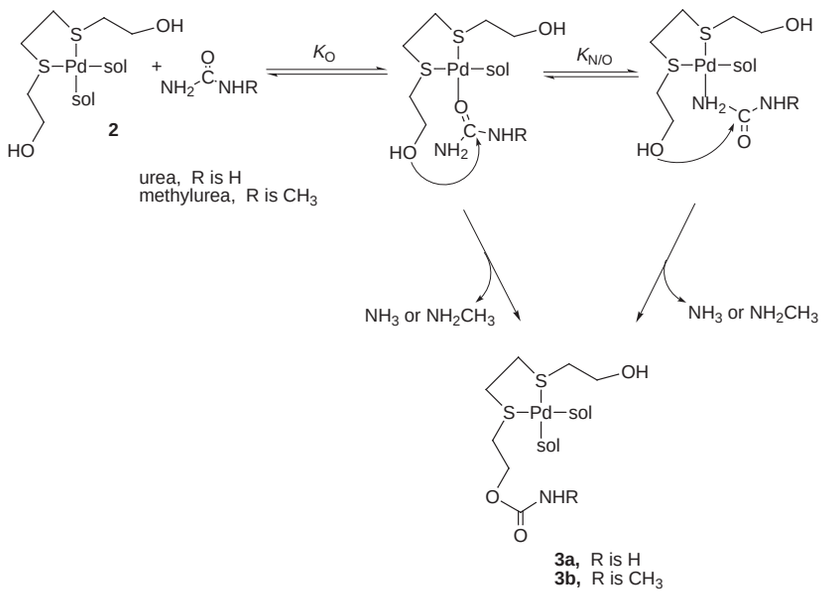


(8)

Table 5 Equilibrium constants for the binding[a] of urea and its derivatives to two palladium(II) complexes and the observed rate constants for alcoholysis

Substrate	*cis*-[Pd(dtod)(sol)$_2$]$^{2+}$				*cis*-[Pd(en)(sol)$_2$]$^{2+}$			
	K_O/M^{-1}	$K_{O/N}$	K_N/M^{-1}	$10^4 k_{obs}$[b]/min^{-1}	K_O/M^{-1}	$K_{O/N}$	K_N/M^{-1}	$10^4 k_{obs}$[c]/min^{-1}
$NH_2C(O)NH_2$[d]	33	0.008	0.3	560 ± 50	31	0.020	0.6	1.46 ± 0.12
$NH_2C(O)NHCH_3$	77	0.005	0.4	580 ± 100[e]	47	0.017	0.8	2.4 ± 1.0
$NHCH_3C(O)NHCH_3$	225	—	—	<0.5[e]	67	—	—	<0.1[f]

[a] The temperature was 273 K unless otherwise stated. [b] For stoichiometric, intramolecular alcoholysis at 313 K. [c] For catalytic, intermolecular ethanolysis at 313 K. Initial concentration of ethanol was 1.5 M. [d] From ref. 5. The equilibrium constants were determined at 313 K. [e] Average from ^{1}H and ^{13}C NMR spectroscopy experiments. [f] Estimated at 313 K.



Scheme 3 Intramolecular, stoichiometric alcoholysis of urea.

(9). Generally, N-bound urea is more activated toward hydrolysis and alcoholysis than is O-bound urea.[4,5]

$$K_O \times K_{O/N} = K_N \quad (9)$$

Co-ordination of 1,3-dimethylurea to *cis*-[Pd(dtod)(sol)$_2$]$^{2+}$ and *cis*-[Pd(en)(sol)$_2$]$^{2+}$ yields only the O-bound isomer. Our finding agrees with the previous reports.[33,34,36]

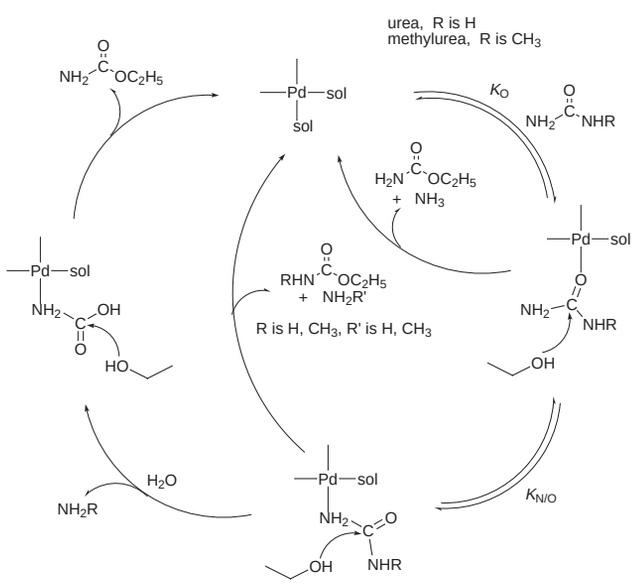
The equilibrium constants, which are average results of multiple experiments by ^{13}C NMR spectroscopy, are given in Table 5. The O-bound isomer is much more abundant than the N-bound isomer. Since N-bound urea is *ca.* 10^7 times more acidic than O-bound urea, the position of the equilibrium between them depends strongly on pH. When the pH is lowered $K_{O/N}$ for urea binding decreases.[5,37] The presence of 1.5 M ethanol in $(CD_3)_2CO$ solution in the bimolecular ethanolysis reactions catalysed by *cis*-[Pd(en)(sol)$_2$]$^{2+}$ does not significantly affect equilibrium constants.[5]

Equilibrium constant K_O and the overall concentration of urea co-ordinated *via* either the O or the N atoms increase as the number of methyl substituents in urea increases and the electron density on the oxygen atom increases. Equilibrium constant $K_{O/N}$ decreases in the same series. This finding is consistent with the results obtained with cobalt(III) complexes.[33]

Unimolecular and bimolecular alcoholysis of urea

Both complexes in Table 5 effect alcoholysis of urea and methylurea. Complex *cis*-[Pd(dtod)(sol)$_2$]$^{2+}$ promotes stoichiometric alcoholysis of co-ordinated urea, according to Scheme 3. The products are the carbamate esters of the dtod ligand, **3a** (75%) and **3b** (25%). Both were observed by ^{13}C NMR spectroscopy after 10 h incubation at 313 K. During the first hour of the reaction, when the initial rates were measured, only **3a**, the product of alcoholysis of the C–NHCH$_3$ bond, was detected. Therefore, the reported k_{obs} values account for the formation of **3a** only.

The complex *cis*-[Pd(en)(sol)$_2$]$^{2+}$ catalyses ethanolysis of co-ordinated urea, according to Scheme 4. This intermolecular



Scheme 4 Intermolecular, catalytic ethanolysis of urea.

reaction involves the external attack of the free alcohol at co-ordinated urea, as shown in Scheme 1.[5] The k_{obs} values in Table 5 show that intramolecular alcoholysis is 240–380 times faster

than the intermolecular ethanolysis. The enhancement of the rate is a result of two factors: proximity of the two reacting species and activation of urea by co-ordination to palladium(II) ion.

Urea co-ordinates to *cis*-$[Pd(en)(sol)_2]^{2+}$ in the presence of *cis*-$[Pd(dtod)Cl_2]$ complex with the equilibrium constant K_O of 14.4 M^{-1}, which is similar to the values in Table 5. There was no ^{13}C NMR spectroscopic evidence for the formation of the binuclear complex $[(en)Pd(\mu\text{-}Cl)_2Pd(dtod)]^{2+}$, which would inhibit urea alcoholysis.[38] Urea co-ordinated to the en complex reacts intermolecularly with the hydroxyl group in the dtod ligand in *cis*-$[Pd(dtod)Cl_2]$. The observed rate constant of 2.9×10^{-4} min^{-1} at 313 K is similar to that for intermolecular ethanolysis and nearly 200 times lower than that for intramolecular alcoholysis in *cis*-$[Pd(dtod)(sol)_2]^{2+}$.

Oxygen-bound 1,3-dimethylurea in either complex in Table 5 does not detectably undergo either intramolecular or catalytic alcoholysis, as Table 5 shows. This unreactivity is not due to the inductive effect of methyl groups, which lowers the electrophilicity of urea because the C–NH_2 bond in urea and the C–$NHCH_3$ bond in methylurea are alcoholysed with similar rate constants. Unreactivity of 1,3-dimethylurea can be attributed to a steric factor; the equilibrium constant $K_{O/N}$ in Scheme 4 is so low that the N-bound isomer, the one that is more reactive in alcoholysis, is practically absent from the reaction mixture.

Conclusion and prospects

The simple palladium(II) complex *cis*-$[Pd(dtod)(sol)_2]^{2+}$ catalyses hydration and methanolysis of nitriles and promotes intramolecular alcoholysis of urea, with rates as much as 10^6 and 10^7 times higher than those of the same reactions in the absence of this complex. All these three reactions are important. Since the dichloromethyl group resembles the vinyl group in its electron-withdrawing ability, our findings on hydration and methanolysis of $CHCl_2CN$ may be relevant to hydration of acrylonitrile, CH_2CHCN. Acrylamide, the product of this reaction, is an important industrial chemical.[22] Cleavage of the amide bond in urea and its derivatives by alcoholysis rather than hydrolysis is interesting for two reasons. First, study of this cleavage may shed light on the action of the nickel enzyme urease.[39] Secondly, a prospect of cleaving amide bonds in proteins by alcoholysis has emerged. Alcoholysis of proteins in non-aqueous solutions would be particularly advantageous for hydrophobic proteins, because their solubility in water precludes the use of hydrolysis.

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